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Frequency of and Factors Associated With Severe Maternal Morbidity

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Abstract

Objective—To estimate the frequency of severe maternal morbidity, assess its underlying etiologies, and develop a scoring system to predict its occurrence.

Methods—This was a secondary analysis of a National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network cohort of 115,502 women and their neonates born in 25 hospitals across the United States over a 3-year period. Women were classified as having severe maternal morbidity according to a scoring system that takes into account the occurrence of red blood cell transfusion (> 3 units), intubation, unanticipated surgical intervention, organ failure, and intensive care unit admission. The frequency of severe maternal morbidity was calculated and the underlying etiologies determined. Multivariable analysis identified patient factors present on admission that were independently associated with severe maternal morbidity, these were used to develop a prediction model for severe maternal morbidity.

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Results—Among 115,502 women who delivered during the study period, 332 (2.9 per thousand births, 95% CI 2.6 – 3.2) experienced severe maternal morbidity. Postpartum hemorrhage was responsible for approximately half of severe maternal morbidity. Multiple patient factors were found to be independently associated with severe maternal morbidity and were used to develop a predictive model with an area under the receiver-operating characteristic curve of 0.80.

Conclusion—Severe maternal morbidity occurs in approximately 2.9 per 1000 births, is most commonly due to postpartum hemorrhage, and occurs more commonly in association with several identifiable patient characteristics.

After years of decline, the frequency of maternal mortality in the United States has begun to increase.¹ Consequently, several professional organizations devoted to maternal health held a meeting in 2012 to determine methods to help improve maternal outcomes.² One concern was the lack of a standardized metric to identify women who experience significant maternal morbidity. This absence hinders both: (1) investigation into etiologies of the events that result in severe morbidity, and (2) evidence-based quality improvement initiatives. Correspondingly, the group called for research that would help to develop a standardized measure of severe maternal morbidity that could be used as the foundation for surveillance and continuous quality improvement.

The development of such a measure is a goal that has been shared by others. Geller et al.³ identified those with very severe morbidity by validating an arithmetical scoring system that took into account whether a woman had an unanticipated surgical intervention, was intubated for more than 12 hours postpartum, received a transfusion more than 3 units, was admitted to the intensive care unit (ICU), or experienced organ failure. However, this measure only has been explored in two studies, both of which were performed in single centers with relatively few patients analyzed.^{4,5}

The purpose of the present study was to estimate the frequency of severe maternal morbidity in a large multi-center obstetric population using the system of Geller et al.,⁴ and to identify its underlying etiologies, associated factors, and whether a scoring system could be developed to predict its occurrence.

Methods

Between 2008 and 2011, investigators at 25 medical centers, belonging to the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network, assembled an obstetric cohort in which detailed information was collected by trained and certified nurses on patient characteristics, intrapartum events, pregnancy outcomes, and postpartum courses of women who delivered at their institutions. Full details of the study design and technique of data collection for the Assessment of Perinatal EXcellence (APEX) cohort have been described previously.⁶ Institutional review board approval was obtained at all centers under a waiver of informed consent.

The present analysis included all women in the APEX cohort. Women were given a score according to the classification system developed by Geller et al.⁴ This system assigns points according to whether a parturient had an unanticipated surgical intervention (1 point), was

intubated for more than 12 hours (2 points), received a red blood cell transfusion of greater than 3 units (3 points), was admitted to the intensive care unit (4 points), or had failure of at least one organ system (5 points). Points are then summated, and those women with 8 or more points are classified as having had severe morbidity. For the present analysis, organ failure was defined as any one of the following: cardiopulmonary arrest, cardiac dysfunction (e.g., cardiomyopathy), adult respiratory distress syndrome (ARDS), pulmonary edema, disseminated intravascular coagulation (DIC), transfusion of platelets, stroke, subdural hematoma, postpartum serum creatinine > 2.0 or postpartum serum AST/SGOT > 1000. Also, women were considered to fulfill the intubation criterion if they were intubated on at least one day, given that data for length of intubation were collected in day, not hour, increments.

Women who experienced severe morbidity were identified and the overall frequency in the cohort was determined. Their abstracted data were further reviewed by one of the investigators (WAG) to determine the primary etiology of their morbid outcome. Etiologic categories included: hemorrhage, infection, hypertensive disorders of pregnancy, non-hypertensive and non-infectious cardiopulmonary complications, trauma, iatrogenic complications, and pre-existing maternal medical conditions.

We then investigated which patient factors were independently associated with severe morbidity using multivariable logistic regression to generate odds ratios and 95% confidence intervals. Model selection and internal validation was performed using k-fold cross-validation in which the cohort was randomly divided into 10 equal parts and logistic regression models, using backward selection, were generated using every possible combination of 9 of the 10 sets.⁷ Variables with $P < .05$ were retained, and each of the 10 sub-samples was used for validation. A risk score was developed using methods similar to Rassi et al.⁸ Each coefficient from the final multivariable model was divided by the smallest coefficient and rounded to the nearest integer. The area under the receiver-operating characteristic curve (AUC), sensitivity, specificity, and positive and negative likelihood ratios (with 95% confidence intervals) were then calculated. All tests were two-tailed and $P < .05$ was used to define statistical significance. No imputation for missing data was performed. Analyses were performed using SAS software (SAS Institute, Cary, NC).

Results

During the study period, 115,502 women delivered. After excluding 7 maternal deaths, 115,495 were included in this analysis. Of the 115,495, 0.5% ($N = 619$) had an unanticipated surgical intervention, 0.1% ($N = 136$) were intubated on at least one day, 0.3% ($N = 323$) received a blood transfusion of at least 3 units, 0.6% ($N = 735$) were admitted to the intensive care unit, and 0.6% ($N = 709$) had at least one organ system fail. The summative point totals, as determined by the system of Geller et al,⁴ are provided in Table 1. Three hundred and thirty-two women (2.9 per thousand births, 95% CI 2.6 – 3.2) had a point total of 8 or more and thus were classified as having had severe morbidity.

Postpartum hemorrhage was responsible for almost half of severe morbidity ($n = 158$, 47.6%). Hypertensive complications ($n = 68$, 20.5%), acute cardiopulmonary complications

(cardiomyopathy, arrest, acute respiratory distress syndrome, pulmonary edema) (n = 63, 19.0%), infection (n = 20, 6.0%), pre-existing maternal medical conditions (n = 8, 2.4%), venous thromboembolism (n = 4, 1.2%), trauma (n = 4, 1.2%), acute neurologic complications (n = 3, 0.9%), iatrogenic events (anaphylaxis, surgical visceral injury)(n = 2, 0.6%), and pregnancy-specific conditions (acute fatty liver, amniotic fluid embolism) (n = 2, 0.6%) accounted for the remainder.

Patient characteristics, stratified by the occurrence of severe morbidity, are presented in Table 2. Patient factors significantly and independently associated with severe morbidity, along with odds ratios and 95% confidence intervals, are presented in Table 3. The presence of placenta accreta was the characteristic most strongly associated with severe morbidity, although multiple other associated factors, such as preterm delivery, antenatal anticoagulant or cigarette use, hypertension, diabetes mellitus, abruptio placentae, and prior cesarean delivery also were identified.

The number of points that each characteristic contributed to the risk score are presented in Table 3. Point totals ranged from 0 to 24, with higher point totals indicating greater frequency of severe maternal morbidity (Table 4). The AUC for the risk score model was 0.80 (95% CI, 0.77–0.83). Sensitivity, specificity, and likelihood ratios for the various risk score cutoff points are also presented (Table 4).

Discussion

In this study, we have used the scoring system developed by Geller et al.⁴ to characterize the frequency and factors associated with severe morbidity in a 25-hospital consortium.⁶ Our results demonstrate that, between 2008 and 2011, severe morbidity occurred in 2.9 per thousand woman who gave birth. Postpartum hemorrhage and hypertensive disorders of pregnancies together accounted for more than two-thirds of the primary underlying causes of severe morbidity. Additionally, the probability of experiencing severe morbidity was related to multiple well-defined patient characteristics.

The observed frequency is slightly lower than that estimated in other reports from developed countries. Wen et al,⁹ using Canadian administrative data, found that severe maternal morbidity occurred in 0.44% of deliveries. Zwart et al,¹⁰ analyzing data from a prospective study between 2004 and 2006, estimated that 0.71% of women giving birth experienced severe maternal morbidity in the Netherlands. Callaghan et al¹¹ studied the National Inpatient Sample to estimate severe maternal morbidity among American women and derived an estimate of 1.5% for the years 2008–2009.

These previous studies differ from the current analysis in several important aspects. Both the Canadian and American estimates were derived from administrative data sets, in which the codes are both limited in their scope, entered primarily for billing, and as Callaghan et al note, subject to errors of omission and commission.^{9,11} Also, the definition of severe morbidity in all of these studies was based on the occurrence of a pre-defined event, such as eclampsia or blood transfusion.^{9–11} However, determining morbidity through such a system could miss women who had severe morbidity because of other diagnoses or causes. These

approaches also may be too sensitive; even though it is likely that a woman who has received a blood transfusion has experienced some morbidity, it may not have been severe.

Our analysis, in contrast, estimated the frequency of severe morbidity from a dataset that was derived from direct chart abstraction and was specifically constructed for research purposes. We used a system that was developed and validated specifically for the purpose of identifying women with the gravest obstetric morbidity. This system is not dependent on any single factor or diagnosis for identification, but on a constellation of adverse outcomes that could be the end result of any serious untoward or precipitating event.

The use of such a system allows insight into the etiologies that are contributing to severe morbidity. Such knowledge is important from a public health perspective in terms of knowing where to focus prevention and treatment efforts. Our data support the concept that postpartum hemorrhage and hypertensive disease of pregnancy are responsible for a large portion of severe maternal morbidity, and underscore that the continued pursuit of best-practice care for these conditions may also yield substantial benefits in terms of decreasing the most severe maternal outcomes.^{12,13}

Our data also allow insight into the patient factors that are associated with severe morbidity. These factors, as well as the risk score derived from them, could be used to help quantify the level of risk a woman has for a severely morbid outcome. It should be noted, however, that this quantification does not allow precise identification of women who will and will not have severe maternal morbidity. Because of the very low prevalence of severe morbidity, as indicated by Table 4, even with a prediction system with an ROC of 0.80, a cutoff point that identifies women with a high risk of severe morbidity will simultaneously miss identifying most women who experience severe morbidity. For example, although a score of at least 19 results in a positive predictive value for severe maternal morbidity of 39%, this cutoff will not identify 93% of women who will experience severe morbidity. Conversely, a cutoff of 5 will result in 67% of women destined to have severe maternal morbidity being identified, but a positive predictive value of only 0.93%. Thus, it is not evident that this prediction model could be used to effectively identify and change the clinical care of individual women.

Nevertheless, as maternal morbidity and mortality increase in frequency in the United States, the need to better understand their risks and causes increases in importance. Without the ability to measure and analyze these outcomes, the potential for systems improvement is compromised.² Severe morbidity as defined in this analysis, was approximately 50 times as frequent as maternal mortality in our population and could be used more readily to track outcomes and to be incorporated into quality improvement initiatives. Our analysis illustrates the importance of gaining a national consensus on a standard definition of severe maternal morbidity in order to allow standardized surveillance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1Frequency of Morbidity Scores Estimated From the System of Geller et al⁴

Score	Frequency	Percent
Unknown*	16	0.01
0	113751	98.49
1	411	0.36
3	93	0.08
4	428	0.37
5	422	0.37
6	24	0.02
7	18	0.02
8	43	0.04
9	130	0.11
10	10	0.01
11	42	0.04
12	25	0.02
13	23	0.02
14	14	0.01
15	45	0.04

} Severe maternal morbidity

* Missing data on components of morbidity score; in nine of these patients, the score was estimated to be less than 8 based on the data available and full range of assumptions regarding the missing data

Table 2

Patient Characteristics by Severe Maternal Morbidity*

	No. (%) in Patients With Severe Maternal Morbidity, n=332	No. (%) in Patients Without Severe Maternal Morbidity, n=115,156	<i>P</i> †
Maternal characteristics			
Age, years			<0.001
< 35	232 (69.9)	95914 (83.3)	
35	100 (30.1)	19242 (16.7)	
Race/ethnicity‡			<0.001
Non-Hispanic White	114 (34.3)	51922 (45.1)	
Non-Hispanic Black	110 (33.1)	23761 (20.6)	
Non-Hispanic Asian	22 (6.6)	5976 (5.2)	
Hispanic	66 (19.9)	27224 (23.6)	
Other	16 (4.8)	5067 (4.4)	
Not documented	4 (1.2)	1206 (1.1)	
Body mass index at delivery, kg/m ²			<0.001
< 25	44 (13.5)	14198 (12.6)	
25–29.9	102 (31.4)	41160 (36.5)	
30–34.9	79 (24.3)	32006 (28.4)	
35–39.9	44 (13.5)	15041 (13.3)	
40	56 (17.2)	10423 (9.2)	
Cigarette use during pregnancy	57 (17.2)	11308 (9.8)	<0.001
Cocaine or methamphetamine use during pregnancy	9 (2.7)	821 (0.7)	<0.001
Insurance status			<0.001
Non-government assisted	159 (48.3)	69284 (60.7)	
Government-assisted	170 (51.7)	44949 (39.4)	
Prenatal care	284 (96.6)	107213 (97.9)	0.11
Obstetric history			<0.001
Nulliparous	123 (37.1)	46646 (40.5)	
Prior vaginal delivery only	92 (27.7)	49769 (43.2)	
Prior cesarean only	43 (13.0)	8827 (7.7)	

	No. (%) in Patients With Severe Maternal Morbidity, n=332	No. (%) in Patients Without Severe Maternal Morbidity, n=115,156	<i>P</i> [†]
Prior cesarean and vaginal	74 (22.3)	9885 (8.6)	
Any hypertension	133 (40.1)	13133 (11.4)	<0.001
Diabetes mellitus			<0.001
None	265 (79.8)	106430 (92.5)	
Gestational	47 (14.2)	6951 (6.0)	
Pregestational	20 (6.0)	1712 (1.5)	
Anticoagulant use during pregnancy	22 (6.6)	895 (0.8)	<0.001
Multiple gestation	30 (9.0)	2785 (2.4)	<0.001
Polyhydramnios	7 (2.1)	933 (0.8)	0.02
Oligohydramnios	15 (4.5)	4684 (4.1)	0.67
Placenta previa	20 (6.0)	447 (0.4)	<0.001
Placenta accreta	41 (12.4)	116 (0.1)	<0.001
Placental abruption	24 (7.2)	906 (0.8)	<0.001
PROM/preterm PROM	19 (6.0)	5983 (5.3)	0.56
GBS status			<0.001
Negative	125 (37.7)	68792 (59.7)	
Positive	51 (15.4)	24335 (21.1)	
Unknown	156 (47.0)	22029 (19.1)	
Neonatal characteristics (on maternal level, according to first born in multiple gestations)			
Presentation at delivery			<0.001
Vertex	272 (82.4)	109421 (95.3)	
Breech	47 (14.2)	4796 (4.2)	
Non-breech malpresentation	11 (3.3)	656 (0.6)	
Gestational age at delivery, weeks			<0.001
23 ⁰ –27 ⁶	28 (8.4)	1055 (0.9)	
28 ⁰ –33 ⁶	57 (17.2)	3508 (3.1)	
34 ⁰ –36 ⁶	82 (24.7)	8871 (7.7)	
37 ⁰ –37 ⁶	34 (10.2)	10395 (9.0)	
38 ⁰ –38 ⁶	32 (9.6)	20311 (17.6)	

	No. (%) in Patients With Severe Maternal Morbidity, n=332	No. (%) in Patients Without Severe Maternal Morbidity, n=115,156	<i>p</i> [†]
39 ⁰ -39 ⁶	52 (15.7)	37553 (32.6)	
40 ⁰ -40 ⁶	30 (9.0)	23832 (20.7)	
41 ⁰ -41 ⁶	16 (4.8)	8981 (7.8)	
42 ⁰	1 (0.3)	651 (0.6)	
Size for gestational age			<0.001
Small	53 (16.0)	10624 (9.2)	
Appropriate	249 (75.2)	95466 (82.9)	
Large	29 (8.8)	9048 (7.9)	

PROM, premature rupture of membranes; GBS, group B streptococcus.

* Severe maternal morbidity defined as a score of at least 8 based on the system of Geller et al.⁴

[†] Based on the chi-square or Fisher's exact test.

[‡] Race or ethnicity as reported in the chart.

Table 3

Adjusted Odds Ratios and 95% Confidence Intervals of Patient Characteristics Associated With Severe Maternal Morbidity*

Patient Characteristic	Adjusted Odds Ratio	95% CI		Risk Score Points [†]
Age 35 years	1.70	1.31	2.21	2
Cigarette use during pregnancy	1.44	1.06	1.96	1
Government-assisted insurance	1.56	1.23	1.98	1
Obstetric history (referent: prior vaginal delivery only)				
Nulliparous	1.38	1.04	1.83	1
Prior cesarean only	1.99	1.35	2.95	2
Prior cesarean and vaginal	2.12	1.52	2.95	2
Any hypertension	3.36	2.61	4.32	4
Diabetes mellitus (referent: no diabetes mellitus)				
Gestational	2.07	1.49	2.88	2
Pregestational	1.63	1.00	2.64	2
Antenatal anticoagulant use	5.21	3.27	8.32	5
Placenta accreta	58.11	36.84	91.64	13
Placental abruption	1.92	1.14	3.24	2
Gestational age at delivery (referent: 39 ⁰ –39 ⁶ weeks)				
23 ⁰ –27 ⁶	9.10	5.52	15.02	7
28 ⁰ –33 ⁶	4.66	3.08	7.06	5
34 ⁰ –36 ⁶	3.15	2.17	4.58	4
37 ⁰ –37 ⁶	1.52	0.97	2.36	1
38 ⁰ –38 ⁶	0.97	0.62	1.51	0
40 ⁰ –40 ⁶	1.09	0.69	1.72	0
41 ⁰ –41 ⁶	1.60	0.90	2.82	1
42 ⁰	1.41	0.19	10.21	1

CI, confidence interval.

* Severe maternal morbidity defined as a score of at least 8 based on the system of Geller et al.⁴

[†] Based on dividing each beta by 0.322, the smallest significant beta (corresponds to nulliparous), and rounding to the nearest integer.

Table 4
 Number (Percent) of Patients and Diagnostic Accuracy of the Risk Score at Various Cutoff Points for Severe Maternal Morbidity

Risk Score	n (%) With Severe Maternal Morbidity	n (%) Without Severe Maternal Morbidity	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
0	4 (0)	10124 (100)				
1	17 (0)	18785 (100)	0.99 (0.97–1.00)	0.09 (0.09–0.09)	1.08 (1.08–1.08)	0.14 (0.08–0.22)
2	31 (0)	24665 (100)	0.94 (0.90–0.96)	0.25 (0.25–0.25)	1.25 (1.25–1.25)	0.25 (0.23–0.28)
3	16 (0)	20827 (100)	0.84 (0.80–0.88)	0.47 (0.47–0.47)	1.59 (1.59–1.59)	0.34 (0.33–0.35)
4	39 (0)	16167 (100)	0.79 (0.75–0.83)	0.65 (0.65–0.66)	2.28 (2.28–2.29)	0.32 (0.31–0.33)
5	28 (0)	8350 (100)	0.67 (0.62–0.72)	0.79 (0.79–0.80)	3.28 (3.27–3.29)	0.41 (0.41–0.42)
6	23 (0)	5138 (100)	0.59 (0.53–0.64)	0.87 (0.87–0.87)	4.44 (4.42–4.46)	0.47 (0.47–0.48)
7	27 (1)	3979 (99)	0.52 (0.46–0.57)	0.91 (0.91–0.91)	5.93 (5.90–5.97)	0.53 (0.52–0.53)
8	30 (1)	2908 (99)	0.44 (0.38–0.49)	0.95 (0.95–0.95)	8.31 (8.25–8.38)	0.60 (0.59–0.60)
9	22 (2)	1434 (98)	0.34 (0.30–0.40)	0.97 (0.97–0.97)	12.79 (12.64–12.94)	0.67 (0.67–0.68)
10	17 (2)	769 (98)	0.28 (0.23–0.33)	0.99 (0.98–0.99)	19.31 (18.99–19.63)	0.73 (0.73–0.73)
11	15 (4)	404 (96)	0.23 (0.18–0.27)	0.99 (0.99–0.99)	29.61 (28.94–30.29)	0.78 (0.78–0.78)
12	6 (3)	187 (97)	0.18 (0.14–0.23)	1.00 (1.00–1.00)	44.09 (42.72–45.50)	0.82 (0.82–0.82)
13	7 (7)	87 (93)	0.16 (0.13–0.21)	1.00 (1.00–1.00)	66.23 (63.75–68.79)	0.84 (0.84–0.84)
14	5 (9)	49 (91)	0.14 (0.11–0.18)	1.00 (1.00–1.00)	83.48 (79.66–87.48)	0.86 (0.86–0.86)
15	5 (12)	38 (88)	0.13 (0.09–0.17)	1.00 (1.00–1.00)	100.00 (94.60–105.71)	0.88 (0.88–0.88)
16	3 (14)	18 (86)	0.11 (0.08–0.15)	1.00 (1.00–1.00)	120.62 (112.76–129.02)	0.89 (0.89–0.89)
17	6 (15)	33 (85)	0.10 (0.07–0.14)	1.00 (1.00–1.00)	134.15 (124.29–144.79)	0.90 (0.90–0.90)
18	5 (22)	18 (78)	0.08 (0.06–0.12)	1.00 (1.00–1.00)	178.96 (161.29–198.56)	0.92 (0.92–0.92)
19	9 (43)	12 (57)	0.07 (0.04–0.10)	1.00 (1.00–1.00)	216.35 (188.36–248.51)	0.93 (0.93–0.93)
20	5 (36)	9 (64)	0.04 (0.02–0.07)	1.00 (1.00–1.00)	198.15 (157.32–249.58)	0.96 (0.96–0.96)
21	5 (38)	8 (62)	0.02 (0.01–0.05)	1.00 (1.00–1.00)	203.25 (138.68–297.88)	0.98 (0.98–0.98)
22	0 (0)	3 (100)	0.01 (0.00–0.03)	1.00 (1.00–1.00)	183.00 (67.94–492.94)	0.99 (0.99–0.99)
23	3 (60)	2 (40)	0.01 (0.00–0.03)	1.00 (1.00–1.00)	305.00 (90.04–1033.20)	0.99 (0.99–0.99)
24	0 (0)	1 (100)				